Remarks

Claim 35 is pending in the subject application. By this amendment, the applicants have amended claim 35 and added new claim 45. Support for the amendments to the claims can be found throughout the subject specification. No new matter has been added by this Amendment. Upon entry of this amendment, claims 35 and 45 are now before the Examiner for consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendments should not be taken to indicate the applicant's agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein is earnestly solicited.

The applicants wish to thank Examiner Natnithithadha for the courtesy extended to the undersigned during the personal Examiner Interview conducted February 9, 2006. This response and the amendments set forth herein are submitted in accordance with the substance of that interview. In addition, the applicants wish to thank Examiner Natnithithadha for bringing to the undersigned's attention references that are being submitted under separate cover in accordance with 37 C.F.R. §§1.56, 1.97, and 1.98. For Examiner Natnithithadha's convenience, the applicants have attached herewith a copy of the Form PTO SB/08A.

As an initial matter, the Amendment filed on August 10, 2005 has been objected to under 35 U.S.C. §132(a) as introducing new matter into the disclosure. The applicants respectfully traverse this objection because new matter was ***not*** introduced via the Amendment of August 10, 2005. Rather, the added material was originally disclosed in ancestral U.S. Applications Serial Nos. 10/178,877 (which has since issued as U.S. Patent No. 6,981,947) and 10/054,619, from which the 10/178,877 application claims priority and is a continuation-in-part application, which were specifically incorporated by reference. For example, both ancestral applications were recited in the "Cross-Reference to a Related Application" section and incorporated by reference in its entirety at page 33 of the subject specification; moreover, the ancestral applications were explicitly incorporated under item 18 of the Utility Patent Application Transmittal form PTO/SB/05. Item 18 specifically supplies the following statement:

> The entire disclosure of the prior application, from which an oath or declaration is supplied...is considered a part of the disclosure of the accompanying continuation...application and is ***hereby incorporated by reference.***

It is a basic premise of patent prosecution practice that essential materials may be incorporated by reference, especially by reference to ***a U.S. patent or pending U.S. application***. Moreover, as noted under §201.06(c) of the MPEP, the inclusion of a statement regarding the incorporation by reference of prior applications (for continuation, divisional, and ***continuation-in-part applications filed under 37 CFR 1.53(b)***) permits an applicant to amend the application to include any subject matter disclosed in such prior applications, without the need for petition.

In this case, the applicants seek to include subject matter that is ***not*** new matter with respect to the subject application. The subject application discloses monitoring the pharmacodynamics and pharmacokinetics of a drug via the analysis of various markers, such as unbound substances, markers, and/or active metabolites associated with the drug, in a sample of the patient's breath (see page 11, lines 14-17 of the subject application). At page 27, line 15 and page 31, lines 1-2, the subject application specifically recites monitoring hypoglycemics (which by definition means "a glucose lowering drug"), such as insulin, via exhaled breath analysis. Glucose is an unbound substance and marker, which can be detected in exhaled breath and tracked to assess the pharmacodynamics and pharmacokinetics of a hypoglycemic, such as insulin. As originally presented and claimed in the ancestral applications (see for example, page 10, paragraph 33 of U.S. Application Serial No. 10/178,877 and claims 33 and 34 of U.S. Application Serial No. 10/054,619), glucose can be detected in exhaled breath and its concentration established. Accordingly, the amendment to the specification and the claims of the subject invention to monitor hypoglycemic (*e.g.*, insulin) administration via analysis of glucose concentration in exhaled breath is ***not*** new matter. Thus, reconsideration and withdrawal of this objection under 35 U.S.C. §132(a) is respectfully requested.

Claim 35 has been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. It is well established in patent law that the claims must be supported by, and interpreted in accordance with, the disclosure of the invention in the application.

The interpretation of claim 35 to detect and measure the concentration glucose in exhaled breath for use in monitoring the administration of glucose lowering drugs is clearly supported by the subject specification, as amended on August 10, 2005.

An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed?" *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). The Office Action notes that the application "does not provide sufficient support for the method step of 'calculating the concentration of endogenous compounds, wherein the endogenous compound is glucose.'" The applicants respectfully submit that claim 35, as currently presented, is clearly supported by the subject specification.

Claim 35 has been amended to clarify a method for monitoring administered glucose lowering drugs via the analysis of the concentration of glucose in exhaled breath. Adequate written description supportive of claim 35 is provided throughout the disclosure including at page 11, lines 14-17; page 27, lines 7-15; page 31, lines 1-2; and in the paragraph inserted (via Amendment dated August 10, 2005) at page 26, beginning at line 21 of the specification and, in particular, with the following phrase: "Moreover, [exhaled breath detection using the method of the present invention] may be used to sense endogenous compounds such as ***glucose***, ketones and electrolytes which are normally found in blood." (emphasis added). As understood by the skilled artisan, glucose can be a marker for a hypoglycemic drug, such as insulin (for example, the skilled artisan readily recognizes that the level of glucose present in blood is indicative of the adequacy of administered insulin). Moreover, glucose is a marker as defined by the subject application (see page 25, lines 16-17 of the subject application wherein "a therapeutic drug marker of the invention provides a means for determining the pharmacodynamics and pharmacokinetics of the drug"). Accordingly, it is respectfully submitted that the applicants have provided description that clearly allows persons of ordinary skill in the art to recognize that the applicants have invented what is claimed. Having met this test, given the teachings of the specification and the scope of the claims as currently presented, the applicants respectfully request the reconsideration and withdrawal of the subject rejection.

Claim 35 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The applicants respectfully submit that the use of the phrase "calculating the concentration of endogenous compounds, wherein the endogenous compound is glucose," does not render claim 35 as indefinite. However, as noted above, the applicants have amended claim 35 to lend greater clarity to the claimed subject matter. As taught in the specification, the concentration of therapeutic markers can be measured in a patient's exhaled breath and used to determine the pharmacodynamics/pharmacodynamics of a drug administered to a patient (see, for example, page 5, lines 11-15 and the entire "Pharmacodynamics and Pharmacokinetics of Therapeutic Drugs" section starting on page 10). Claim 35 now recites the monitoring of glucose lowering drugs via the calculation of glucose concentration in exhaled breath. Accordingly, reconsideration and withdrawal of this rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claim 35 has been rejected under 35 U.S.C. §102(b) as being anticipated by Ueda *et al.* (U.S. Patent No. 5,425,374). The applicants respectfully traverse this rejection because the Ueda *et al.* reference is totally unrelated to the claimed subject matter, namely monitoring the administration of hypoglycemics via the detection of glucose in exhaled breath.

There is ***no*** teaching or suggestion by Ueda *et al.* to detect the presence of ***glucose*** in exhaled breath. Specifically, the Ueda *et al.* reference teaches the use of exhaled breath for the detection of ***ketone bodies***. The Ueda *et al.* reference indicates that the presence of ketone bodies in breath are ***at best*** a means for merely "screening" (paragraph 8, line 66) subjects for diabetes. There is not indication by Ueda *et al.* that the presence and concentration of ***glucose*** in exhaled breath can be used to monitor the pharmacokinetics and/or pharmacodynamics of hypoglycemics. In fact, the detection of ketone bodies in breath is a very poor and late indication of diabetes because the ketones may be the result of diabetes (actually only in the presence of diabetic ketoacidosis) ***or*** may be indicative of fasting and malnutrition.

The claimed technology is quite different and subsequently more advantageous than the technology of Ueda *et al.* Claim 35, as currently presented, recites the use of sensor technology to detect ***glucose*** in exhaled breath to aid in monitoring the administration of a hypoglycemic to a patient. As disclosed in the subject application, the concentration of unbound substances and

markers (such as glucose) in exhaled breath that are associated with drug can be used to accurately correlate with blood glucose concentrations, and thus determine and ensure proper hypoglycemic dosing regimens. Because, in accordance with the present invention, the use of exhaled breath detection of glucose is non-invasive, testing of blood glucose to assess the pharmacokinetics and/or pharmacodynamics of a hypoglycemic can be more frequently performed, subsequently enabling better glucose control.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra; Kalman v. Kimberly-Clarke*, 713 F.2d 760 (Fed. Cir. 1983)] (emphasis added).

In *Dewey v. Almy Chem. Co. v. Mimex Co.*, Judge Learned Hand wrote:

> No doctrine of the patent law is better established than that a prior patent . . . to be an anticipation must bear within its four corners adequate directions for the practice [of the subsequent invention] . . . if the earlier disclosure offers no more than a starting point . . . if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. 124 F.2d 986, 990 (2nd Cir. 1942).

As noted above, the Ueda *et al.* reference does not disclose monitoring the administration of a hypoglycemic via the detection of glucose in exhaled breath. Thus, under the applicable statutory and case law, the Ueda *et al.* reference does not anticipate the current applicants' claim 35. Therefore, reconsideration and withdrawal of the rejection under 35 USC §102(b) is respectfully requested.

Please note that the references (U.S. Patent Application Nos. 09/940,750 and 10/363,577 and International Application No. PCT/US01/41917) cited in the Information Disclosure Statement

submitted herewith are merely directed to systems and methods for detecting certain analytes in exhaled breath. There is no description in these references regarding monitoring the administration of a hypoglycemic to a patient via the detection and calculation of the amount of glucose in exhaled breath. Accordingly, the applicants respectfully submit that the references cited in the Information Disclosure Statement are not pertinent to the subject matter of the pending claims.

In addition, the applicants would like to bring to the Examiner's attention a Petition to delete Drs. Chris Sackellares and Mark Gold as inventors, which was filed on December 15, 2005. The applicants note that, to date, the Petition has not been entered in PAIR. The applicants would also like to notify the Examiner that they are also in the process of adding Dr. David Bjoraker as an inventor. The Examiner's attention to these matters is greatly appreciated.

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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